(a)	exposing an in vivo region of a subject to a magnetic polarizing field, the in
vivo region includi	ng non-neural tissue and a nerve, the nerve being a member of the group consisting
of peripheral nerve	s, cranial nerves numbers three through twelve, and autonomic nerves;

- (b) exposing the *in vivo* region to an electromagnetic excitation field;
- (c) producing an output indicative of the *in vivo* region's resonant response to the polarizing and excitation fields;
- (d) controlling the performance of the steps (a), (b), and (c) to enhance, in the output produced, the selectivity of said nerve, while the nerve is living in the *in vivo* region of the subject; and
- (e) processing the output to generate a data set describing the shape and position of said nerve, said data set distinguishing said nerve from non-neural tissue in the *in vivo* region to provide a conspicuity of the nerve that is at least 1.1 times that of the non-neural tissue, without the use of neural contrast agents.

The method of Claim 89, wherein said data set distinguishes said nerve from non-neural tissue in the *in vivo* region so that said data set describes the nerve at an intensity at least 5 times that of the non-neural tissue.

The method of Claim 89, wherein the step of exposing the *in vivo* region to a polarizing field includes the step of exposing the *in vivo* region to a polarizing field including at least one diffusion-weighted gradient.

The method of Claim 91, wherein the at least one diffusion-weighted gradient includes a first gradient substantially parallel to the nerve and a second gradient substantially perpendicular to the nerve, and the step of producing an output includes the steps of producing a first output when the first gradient is employed and a second output when the second gradient is employed, and the step of processing the output includes the step of subtracting the first output from the second output.

The method of Claim 92, wherein the step of subtracting further includes the step of determining the registration between the first output and the second output.

The method of Claim 93, wherein said method includes the step of inhibiting the step of subtracting unless a threshold level of registration is exhibited between the first and second outputs.

The method of Claim 92, wherein the non-neural tissue includes fat, and prior to exposing the *in vivo* region to said first and second gradients, the *in vivo* region is exposed to electromagnetic fields that suppress the contribution of the fat in said first and second outputs.

The method of Claim 91, wherein the at least one diffusion-weighted gradient includes a predetermined arrangement of gradients, the step of producing an output includes the step of producing a separate output associated with each gradient, and the step of processing the output includes the steps of vector processing the separate outputs to generate data representative of anisotropic diffusion exhibited by the nerve, and processing said data representative of anisotropic diffusion to generate said data set describing the shape and position of the nerve.

The method of Claim 89, wherein the non-neural tissue includes fat, and the steps of exposing the *in vivo* region to an excitation field and producing an output involve the excitation of any fat in the *in vivo* region in a manner designed to suppress the contribution of the fat to the output.

The system of Claim 97, wherein the contribution of fat is suppressed by employing a chemical shift selective sequence.

The method of Claim 97, wherein the step of processing further includes the step of analyzing the output for information representative of fascicles found in peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves.

The method of Claim 99, wherein the step of processing further includes using the results of said step of analyzing the output for information representative of fascicles to suppress from said data set tissue that is not fascicular.

1

101. The method of Claim 89, wherein the step of processing further includes the step of analyzing the output for information representative of fascicles found in peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves.

The method of Claim 401, wherein the step of processing further includes using the results of said step of analyzing the output for information representative of fascicles to suppress from said data set tissue that is not fascicular.

The method of Claim 89, wherein said step (d) is used to exploit a characteristic spin-spin relaxation coefficient of peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves, said spin-spin relaxation coefficient of these nerves being substantially longer than that of other surrounding issue.

104. The method of Claim 103, wherein the steps of exposing the *in vivo* region to an excitation field and producing an output are separated by an echo time that is greater than 60 milliseconds to enhance the distinction of said nerve from non-neural tissue in the *in vivo* region.

105. The method of Claim 104, wherein the non-neural tissue includes muscle that is suppressed by said step (d), by exploiting the characteristic spin-spin relaxation coefficient of peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves.

The method of Claim 104, wherein the step of exposing the *in vivo* region to an excitation field is repeated after a repetition time that is greater than one second to enhance the distinction of said nerve from the non-neural tissue in the *in vivo* region.

107. The method of Claim 104, wherein the non-neural tissue includes fat and prior to said step (c), the *in vivo* region is exposed to electromagnetic fields that suppress the contribution of the fat in said output.

108. The method of Claim 89, wherein the step (d) causes said step (b) of exposing the in vivo region to an excitation field to induce a magnetization transfer from non-anisotropically diffusing

25

water in the *in vivo* region to anisotropically diffusing water in said nerve, to more readily distinguish the nerve from non-neural tissue.

109. The method of Claim 108, wherein the non-neural tissue includes fat and prior to said step (c), the *in vivo* region is exposed to electromagnetic fields that suppress the contribution of the fat in said output.

The method of Claim 89, wherein the *in vivo* region may includes blood vessels and said step (d) suppresses the blood vessels from said data set.

The method of Claim 110, wherein said steps (a), (b), and (c) are repeated to produce a first output in which the contribution of nerve is enhanced and as second output in which the contribution of blood vessels is enhanced, and said step (e) of processing the output includes the step of processing the first and second outputs to suppress the blood vessels from said data set.

112. The method of Claim 89, wherein if the non-neural tissue in said in vivo region includes blood vessels and cerebrospinal fluid, said step (d) suppresses the blood vessels and the cerebrospinal fluid from said data set.

113. The method of Claim 89, wherein said step (d) suppresses the influence of motion of the *in vivo* region on said data set.

The method of Claim 89, wherein said method further includes the step of immobilizing the *in vivo* region in a splint to reduce motion artifact in said data set.

The method of Claim 89, wherein the *in vivo* region includes a plurality of peripheral nerves, cranial nerves numbers three through twelve, or autonomic nerves, and said method further includes the step of administering a contrast agent to a selected one of the plurality of peripheral nerves, cranial nerves numbers three through twelve, or autonomic nerves to remove said selected one nerve from said data set.

116. The method of Claim 89, wherein said steps (a) through (c) include the step of exposing the *in vivo* region to a readout gradient rephasing pulse and a slice-selective excitation

1

pulse, said readout gradient rephasing pulse being generated directly before said output is produced, instead of directly after the generation of the slice-selective excitation pulse, so as to reduce the appearance of undesirable cross-terms in said data set.

The method of Claim 116, wherein said steps (a) through (c) further include the step of exposing the *in vivo* region to a two-part phase encoding gradient, so as to further reduce the appearance of undesirable cross-terms in said data set.

The method of Claim 89, wherein the intensity of said nerve in said data set is at least 10 times that of non-neural tissue in the *in vivo* region.

The method of Claim 189, wherein said method further includes the step of processing said data set to generate an image displaying the shape and position of said nerve.

A method of utilizing magnetic resonance to determine the shape and position of a structure, said method including the steps of:

- (a) exposing a region to a magnetic polarizing field including a predetermined arrangement of diffusion-weighted gradients, the region including a selected structure that exhibits diffusion anisotropy and other structures that do not exhibit diffusion anisotropy;
  - (b) exposing the region to an electromagnetic excitation field;
- (c) for each of said diffusion-weighted gradients, producing an output indicative of the region's resonant response to the excitation field and the polarizing field including the diffusion-weighted gradient; and
- (d) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by said selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and
- (e) / processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set

4

5

6

9

10

11

19

20

distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy.

The method of Claim 120, wherein said selected structure is neural tissue in a mammal and said other structures are non-neural tissue in the mammal.

The method of Claim 121, wherein said step of processing said data representative of anisotropic diffusion includes the steps of:

analyzing said data representative of anisotropic diffusion to determine an effective direction of the anisotropic diffusion exhibited by said neural tissue, so as to determine an optimal orientation for diffusion-weighted gradients;

exposing the region to two additional diffusion-weighted gradients respectively substantially parallel to and substantially perpendicular to said effective direction;

producing two additional outputs indicative of the region's resonant responses respectively to said two additional diffusion-weighted gradients; and

calculating a difference between said two additional outputs to generate said data set describing the shape and position of said neural tissue.

The method of Claim 121, wherein said data set describing the shape and position of said neural tissue describes the shape and position of a selected cross section of said neural tissue, and the steps used to generate said data set are repeated to generate additional data sets describing different cross sections of said neural tissue, and a further data set that describes the three dimensional shape and position of a segment of said neural tissue is generated by steps including:

analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said neural tissue; and

based upon the results of said step of analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that



describes the three dimensional shape and position of the segment of said neural tissue, thereby enabling the three dimensional shape and position of curved neural tissue to be described.

The method of Claim 123, wherein said step of analyzing the data representative of anisotropic diffusion includes determining an effective direction of the anisotropic diffusion exhibited by said neural tissue in each of said selected and different cross sections.

The method of Claim 121, wherein said predetermined arrangement of gradients includes first, second, and third orthogonal gradients, and said data representative of anisotropic diffusion include a description of an effective vector representative of the anisotropic diffusion exhibited by said neural tissue.

The method of Claim 125, wherein said data set describing the shape and position of said neural tissue is based upon the length of said effective vector.

The method of Claim 126, wherein the step of exposing the region to a magnetic polarizing field includes the step of exposing the region to a zero diffusion gradient polarizing field that does not include a diffusion-weighted gradient, the step of producing an output includes the step of producing a zero diffusion gradient output indicative of the region's resonant response to said zero diffusion gradient polarizing field, and the length of said effective vector is normalized by a magnitude of said zero diffusion gradient output.

The method of Claim 125, wherein said data set describing the shape and position of said neural tissue is based upon an angle describing in part the direction of said effective vector.

The method of Claim 125, wherein said step of processing said data representative of anisotropic diffusion includes the steps of:

exposing the region to two additional diffusion-weighted gradients respectively substantially parallel to and substantially perpendicular to the direction of said effective vector representative of the anisotropic diffusion exhibited by said neural tissue;

2

3

4

5

6

12

-60

producing two additional outputs indicative of the region's resonant responses respectively to said two additional diffusion-weighted gradients; and

calculating a difference between said two additional outputs to generate said data set describing the shape and position of said neural tissue.

The method of Claim 125, wherein said data set describes the shape and position of a selected cross section of said neural tissue, and the steps used to generate said data set are repeated to generate additional data sets describing different cross sections of said neural tissue, and a further data set that describes the three dimensional shape and position of a segment of said neural tissue is generated by steps including:

analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said neural tissue; and

based upon the results of said step of analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said neural tissue, thereby allowing the three dimensional shape and position of curved neural tissue to be described.

The method of Claim 130, wherein said step of analyzing the data representative of anisotropic diffusion includes the step of analyzing the direction of the effective vector representative of the anisotropic diffusion exhibited by said neural tissue in each of said cross sections.

The method of Claim 126, wherein said step of processing said data representative of anisotropic diffusion includes the steps of:

analyzing said data representative of anisotropic diffusion to determine an effective direction of the anisotropic diffusion exhibited by said selected structure, so as to determine an optimal orientation for diffusion-weighted gradients;

exposing the region to two additional diffusion-weighted gradients respectively substantially parallel to and substantially perpendicular to said effective direction;

producing two additional outputs indicative of the region's resonant responses respectively to said two additional diffusion-weighted gradients; and

calculating a difference between said two additional outputs to generate said data set describing the shape and position of said selected structure.

The method of Claim 120, wherein said data set describing the shape and position of said selected structure describes the shape and position of a selected cross section of said selected structure, and the steps used to generate said data set are repeated to generate additional data sets describing different cross sections of said selected structure, and a further data set that describes the three dimensional shape and position of a segment of said selected structure is generated by steps including:

analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said selected structure; and

based upon the results of said step of analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes a three dimensional shape and position of the segment of said selected structure, thereby allowing the three dimensional shape and position of a curved structure exhibiting anisotropic diffusion to be described.

The method of Claim 120, wherein said predetermined arrangement of gradients includes first, second, and third orthogonal gradients, and said data representative of anisotropic diffusion include a description of an effective vector representative of the anisotropic diffusion exhibited by said selected structure.

-11-

LAW OFFICES OF

1/4	135. A method of utilizing magnetic resonance to determine data representative of diffusion
$/_2$	anisotropy exhibited by a structure, said method including the steps of:
3	(a) exposing a region to a suppression sequence of electromagnetic fields that
4	suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion
5	anisotropy, so as to/increase the apparent diffusion anisotropy of structures in the region that exhibit
6	diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-
7	weighted magnetic gradients;
8	(b) exposing the region to a predetermined arrangement of diffusion-weighted
9	magnetic gradients, said predetermined arrangement of diffusion-weighted magnetic gradients chosen
10	to:
11	i) emphasize a selected structure in the region exhibiting diffusion
12	anisotropy in a particular direction; and
13	suppress other structures in the region exhibiting diffusion anisotropy in
14	directions different from said particular direction;
15	(c) for each of said diffusion-weighted gradients, producing an output indicative of
16	the region's resonant response to the diffusion-weighted gradient; and
17	(d) processing said outputs to generate data representative of the diffusion
18,	anisotropy of the selected structure.
19	The method of Claim 135, wherein said data representative of the diffusion anisotropy
20	of the selected structure is processed to produce a data set that describes the shape and position of
21	the selected structure.  53.7  The method of Claim 136, wherein the selected diffusion anisotropic structure is
22	, and the control of
23	neural tissue in vivo and living.
24	
25	

1

The method of Claim 136, wherein the selected diffusion anisotropic structure is a member of the group consisting of peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves, and is living.

- 139. A magnetic resonance apparatus for determining the shape and position of mammal tissue, said apparatus including:
- magnetic polarizing field, the *in vivo* region including non-neural tissue and a nerve, the nerve being a member of the group consisting of peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves;
- (b) an excitation and output arrangement for exposing the subject to an electromagnetic excitation field;
- source and said excitation and output arrangement so that the polarizing field and the excitation field cooperatively induce a resonant response in the *in vivo* region to enhance the selectivity of said nerve while the nerve is *in vivo* and living, said excitation and output arrangement further for producing an output indicative of the resonant response of the *in vivo* region at a time determined by said sequence controller, and
- a processor for processing said output to produce a data set describing the shape and position of said nerve, said data set distinguishing the nerve from non-neural tissue in the *in vivo* region to provide a conspicuity of the nerve that is at least 1.1 times that of the non-neural tissue, without requiring the use of neural contrast agents.
- 140. The apparatus of Claim 139, wherein said excitation and output arrangement includes a phased-array coil system.
- 141. The apparatus of Claim 139, wherein said apparatus further includes a splint for substantially immobilizing the *in vivo* region.

(206) 682-8100

- 142. The apparatus of Claim 141, wherein said splint includes at least one marker for relating the position of said splint to said region of the subject.
- 143. The apparatus of Claim 142, wherein said splint is constructed to reduce edge effects that might otherwise influence said data set describing the shape and position of the nerve.
- 144. The apparatus of Claim 139, wherein said apparatus is coupleable to an auxiliary data collection system constructed to collect information regarding non-neural structure, the information being used by said processor to enhance the degree by which said data set describing the shape and position of the nerve distinguishes non-neural tissue in the *in vivo* region.
- 145. The apparatus of Claim 139, wherein said apparatus is coupleable to a diagnostic system constructed to analyze said data set to detect a neural condition of interest.
- 146. The apparatus of Claim 139, wherein said apparatus is coupleable to a therapeutic system.
  - 147. The apparatus of Claim \139, wherein said apparatus is coupleable to a surgical system.
- 148. The apparatus of Claim 39, wherein said apparatus is coupleable to a development system.
- 149. The apparatus of Claim 139, wherein said apparatus further includes an output device for displaying an image of the nerve based on said data set.
- A magnetic resonance apparatus for determining the shape and position of a structure, said apparatus including:
- (a) a polarizing field source for exposing a region to a magnetic polarizing field including a predetermined arrangement of diffusion-weighted gradients, the region including a selected structure that exhibits diffusion anisotropy and other structures that do not exhibit diffusion anisotropy;
  - (b) an excitation and output arrangement for:
    - i) exposing the region to an electromagnetic excitation field; and

ii)	prod	lucing,	for	each	of	said	diffusi	on-weigh	ted	gradients,	an	output
ndicative of the region's	resonant i	respons	se to	the ex	xcit	ation	field as	nd the pol	lariz	ing field in	clud	ing the
diffusion-weighted gradie	nt; and											

## (c) a processor for:

i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and

processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy.

The apparatus of Claim 150, wherein said selected structure is neural tissue in a mammal and said other structures are non-neural tissue in the mammal.

The apparatus of Claim 151, wherein:

said processor is further for analyzing said data representative of anisotropic diffusion to determine an effective direction of the anisotropic diffusion exhibited by said neural tissue, so as to determine an optimal orientation for diffusion-weighted gradients:

said polarizing field source is further for exposing the region to two additional diffusionweighted gradients respectively substantially parallel to and substantially perpendicular to said effective direction:

said excitation and output arrangement is further for producing two additional outputs indicative of the region's resonant responses respectively to said two additional diffusion-weighted gradients; and

said processor is further for determining the difference between said two additional outputs to generate said data set describing the shape and position of said neural tissue.

The apparatus of Claim 151, wherein said data set describing the shape and position of said neural tissue describes the shape and position of a selected cross section of said neural tissue, and said apparatus is further for generating additional data sets describing different cross sections of said neural tissue, and said processor is further for calculating a further data set that describes the three dimensional shape and position of a segment of said neural tissue by:

analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said neural tissue; and

based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said neural tissue, thereby allowing a three dimensional shape and position of curved neural tissue to be described.

The apparatus of Claim 151, wherein said predetermined arrangement of gradients includes first, second, and third orthogonal gradients, and said data representative of anisotropic diffusion include a description of an effective vector representative of the anisotropic diffusion exhibited by said neural tissue.

The apparatus of Claim 150, wherein:

said processor is further for analyzing said data representative of anisotropic diffusion to determine an effective direction of the anisotropic diffusion exhibited by said selected structure, so as to determine an optimal orientation for diffusion-weighted gradients;

said polarizing field source is further for exposing the region to two additional diffusionweighted gradients respectively substantially parallel to and substantially perpendicular to said effective direction;

25

said excitation and output arrangement is further for producing two additional outputs indicative of the region's resonant responses respectively to said two additional diffusion-weighted gradients; and

said processor is further for determining a difference between said two additional outputs to generate said data set describing the shape and position of said selected structure.

The apparatus of Claim 150, wherein said data set describing the shape and position of said selected structure describes the shape and position of a selected cross section of said selected structure, and said apparatus is further for generating additional data sets describing different cross sections of said selected structure, and said processor is further for determining a further data set that describes the three dimensional shape and position of a segment of said selected structure by:

analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said selected structure; and

based upon the results of said analyzing the data representative of anisotropic diffusion, combining/said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said selected structure, thereby enabling a three dimensional shape and position of curved structure exhibiting anisotropic diffusion to be described.

The apparatus of Claim 150, wherein said predetermined arrangement of gradients includes first, second, and third orthogonal gradients, and said data representative of anisotropic diffusion include a description of an effective vector representative of the anisotropic diffusion exhibited by said selected structure.

158. A magnetic resonance apparatus for determining data representative of the diffusion anisotropy exhibited by a structure, said apparatus including:

LAW OFFICES OF

- (a) an excitation and output arrangement for exposing a region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted magnetic gradients;
- (b) a polarizing field source for exposing the region to a predetermined arrangement of diffusion-weighted magnetic gradients chosen to:
- i) emphasize a selected structure in the region exhibiting diffusion anisotropy in a particular direction; and
- suppress other structures in the region exhibiting diffusion anisotropy in directions different from said particular direction, said excitation and output arrangement further for producing, for each of said diffusion-weighted gradients, an output indicative of the region's resonant response to the diffusion-weighted gradient; and
- (c) a processor for processing said outputs to generate data representative of the diffusion anisotropy of the selected structure.

The apparatus of Claim 183, wherein said processor is further for processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure.

O \$160. The apparatus of Claim 159, wherein the selected diffusion anisotropic structure is neural tissue and is living.

The apparatus of Claim 19, wherein the selected diffusion anisotropic structure is a member of the group consisting of peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves, and is living.--